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**FACSIMILE TRANSMITTAL**

**TO**

**Name:** Mr. Mark Polutta
**Firm:** U.S. Patent and Trademark Office
**Fax No.:** (571) 273-7709
**Subject:** U.S. Patent Application No. 10/510,019

**Phone No.:** (571) 272-7709
**Date:** August 2, 2007

**FROM**

**Name:** Erin Sommers
**Fax # Verified by:** E. Sommers @ MD 826
**Our File No.:** 06267.0124-00000

**Phone No.:** (202) 408-4292
**# Pages (incl. this):** 6

**Confirmation Copy to Follow: NO**

**MESSAGE:**

**Mark: Per our telephone conversation this morning, here are the 4 marked up pages of U.S. Patent Application Publication No. 2006/0094740 that were submitted with the entire publication on June 27, 2006. Specifically, pages 6, 7, 24, and 27 are enclosed. In addition, a copy of the stamped postcard is included.**

BCD/SJS/VS

14

**PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:**

In Re Application of: David DIN BELLE et al.

Application No.: 10/510,019 Group Art Unit: 1615

Filed: May 31, 2005 Examiner: UNKNOWN

For: POLYCYCLIC COMPOUNDS AS POTENT ALPHA2-ADRENOCEPTOR ANTAGONISTS

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1. Request for Corrected Patent Application Publication Under 37 C.F.R. §1.221(b) (2 pages);
2. Inserts to Application Publication (2 pages); and
3. Copy of application publication with markings (36 pages)

Dated: June 27, 2006

Docket No.: 06267.0124

SJS/V. Simmons - Mail Drop 1034


(Due Date: July 4, 2006)

Mailed 6/28/06

Ethyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-a] quinolizin-2-yl)-methanol, (1-αEthyl-1,2,3,4,6,7,12,12bβ-octahydroindolo[2,3-a]quinolizin-1-ylmethoxy)-acetic acid ethyl ester, 1-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-a]quinolizin-2-yl)-ethanone, 1-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-a]quinolizin-2-yl)-ethanol, 2-(2α-ethyl-1,2,3,4,6,7,12,12bα-octahydro-indolo[2,3-a] quinolizin-2-yl)-propan-2-ol, 2-(3-ethyl-1,2α,3α,4,6,7,12, 12bαX-octahydro-indolo[2,3-a]quinolizin-2-yl)-propan-2-ol, (3-ethyl-2-methy-1α,2β,3β,4,6,7,12,12bβ-octahydro-indolo[2,3-a]quinolizin-1-yl)-methanol, 3-ethyl-1,2-dimethyl-1α,2β,3β,4,6,7,12,12bβ-octahydro-indolo[2,3-a] quinolizine, 1,2-dimethyl-1,2,3,4,6,7,12,12bβ-octahydro-indolo[2,3-a]quinolizin-1β-ol, (1-ethyl-2-methyl-1β,2β,3β, 3β4,6,7,12,12bα-octahydro-indolo[2,3-a]quinolizin-3-yl)-methanol or 1-β-Hydroxymethyl-1-methyl-1,2,3,4,6,7,12, 12bβ-octahydro-indolo[2,3-a]quinolizine-6β-carboxylic acid methyl ester.

[0078] The terms employed herein have the following meanings:

[0079] The term "halo" or "halogen", as employed herein as such or as part of another group, refers to chlorine, bromine, fluorine or iodine.

[0080] The term "carboxyl", as employed herein, refers to a —COOH group.

[0081] The term "aryl", as employed herein as such or as part of another group, refers to a monocyclic or bicyclic aromatic group containing 6 to 12 carbon atoms. Representative examples of aryl include, but are not limited to, phenyl, naphthyl, and the like.

[0082] The term "aryl($C_1$-$C_6$)alkyl", as employed herein as such or as part of another group, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein.

[0083] The term "aryloxy", as employed herein as such or as part of another group, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an —O— group.

[0084] The term "aryl($C_1$-$C_6$)alkoxy", as employed herein as such or as part of another group, refers to an aryl group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkoxy group, as defined herein.

[0085] The term "aryloxy($C_1$-$C_6$)alkyl, as employed herein, refers to an aryloxy group, as defined herein, appended to the parent molecular moiety through an $C_1$-$C_6$)group, as defined herein.

[0086] The term "aryl($C_1$-$C_6$)alkyl, as employed herein, refers to an aryl($C_1$-$C_6$)alkoxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein.

[0087] The term "hydroxy", as employed herein as such or as part of another group, refers to an —OH group.

[0088] The term "hydroxy($C_1$-$C_6$)alkyl", as employed herein as such or as part of another group, refers to at least one hydroxy group, as defined herein, appended to the parent molecular moiety through a ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of hydroxy($C_1$-2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 1-hydroxypropyl, 1-methyl-1-hydroxyethyl, 1-methyl-1-hydroxypropyl, and the like.

[0089] The term "halo($C_1$-$C_6$)alkyl", as employed herein, refers to one or more halogen, as defined herein, appended to the parent molecular moiety through a ($C_1$-

[0090] The term "aryloxy($C_1$-$C_6$)alkyl, as employed herein, refers to an aryloxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein.

[0091] The term "aryl($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, as employed herein, refers to an aryl($C_1$-$C_6$)alkoxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein.

[0092] The term "hydroxy", as employed herein as such or as part of another group, refers to an —OH group.

[0093] The term "hydroxy($C_1$-$C_6$)alkyl", as employed herein as such or as part of another group, refers to at least one hydroxy group, as defined herein, appended to the parent molecular moiety through a ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of hydroxy($C_1$-$C_6$)alkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 1-hydroxypropyl, 1-methyl-1-hydroxyethyl, 1-methyl-1 -hydroxypropyl, and the like.

[0094] The term "halo($C_1$-$C_6$)alkyl", as employed herein, refers to one or more halogen, as defined herein, appended to the parent molecular moiety through a ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of halo($C_1$-$C_6$)alkyl include, but are not limited to, fluoromethyl, difluoromethyl, trifluoromethyl, 2-chloroethyl, 3-bromopropyl, and the like.

[0095] The term "amino", as employed herein as such or as part of another group, refers to a —$NH_2$ group.

[0096] The term "amino($C_1$-$C_6$)alkyl", as employed herein, refers to an amino group, as defined herein, appended to the parent molecular moiety through a ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of amino($C_1$-$C_6$)alkyl include, but are not limited to, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 2-aminopropyl, 4-aminobutyl, 1-methyl-1-aminoethyl, and the like.

[0097] The term "mono- or di($C_1$-$C_6$)alkylamino", as employed herein as such or as part of another group, refers to one or two ($C_1$-$C_6$)alkyl group(s), as defined herein, appended to the parent molecular moiety through an amino group, as defined herein. Representative examples of mono- or di($C_1$-$C_6$)alkylamino include, but are not limited to methylaamino, ethylamino, propylamino, butylamino, dimethylamino, diethyl-amino, N-ethyl-N-methylamino, and the like.

[0098] The term "mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl", as employed herein, refers to a mono- or di($C_1$-$C_6$)alkylamino group, as defined herein, appended to the parent molecular moiety through a ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl include, but are not limited to, N,N-dimethylaminomethyl, N,N-diethylaminomethyl, N-methylamninoethyl, N-methylaminopropyl, N-ethyl-N-

[0099] The term "($C_1$-$C_6$)alkoxy", as employed herein as such or as part of another group, refers to a ($C_1$-$C_6$)alkyl, as defined herein, appended to the parent molecular moiety through an -O- group. Representative examples of ($C_1$-$C_6$)alkoxy include, but are not limited to methoxy, ethoxy, propoxy, butoxy, isobutoxy, sec-butoxy, tert-butoxy, and the like.

[0100] The term "($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl", as employed herein as such or as part of another group, refers to at least one ($C_1$-$C_6$)alkoxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein. Representative examples of ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl include, but are not limited to methoxymethyl, ethoxymethyl, 2-methoxyethyl, 2-ethoxyethyl, 3,3-dimethoxypropyl, 2,4-dimethoxybutyl and the like.

[0101] The term "hydroxy($C_1$-$C_6$)alkoxy", as employed herein as such or as part of another group, refers to a hydroxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-C6)alkoxy group, as defined herein.

[0102] The term "hydroxy($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, as employed herein, refers to a hydroxy($C_1$-$C_6$)alkoxy group, as defined herein, appended to the parent molecular moiety through an ($C_1$-$C_6$)alkyl group, as defined herein.

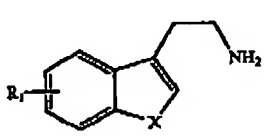
[0103] The term "carbamoyl", as employed herein as such or as part of another group, refers to a —$CONH_2$ group.

[0104] ~~The term "mono- or di($C_1$-$C_6$)-alkylcarbamoyl", as employed herein, refers to one or two ($C_1$-$C_6$)alkyl group(s), as defined herein, appended to the parent~~ See attachment Insert B

[0105] Pharmaceutically acceptable salts, e.g. acid addition salts with both organic and inorganic acids are well known in the field of pharmaceuticals. Non-limiting examples of these salts include chlorides, bromides, sulfates, nitrates, phosphates, sulfonates, formates, tartrates, maleates, citrates, benzoates, salicylates and ascorbates. Pharmaceutically acceptable esters, when applicable, may be prepared by known methods using pharmaceutically acceptable acids that are conventional in the field of pharmaceuticals and that retain the pharmacological properties of the free form. Non-limiting examples of those esters include esters of aliphatic or aromatic alcohols, e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl esters.

[0106] The compounds of the invention can be prepared analogously or according to the methods known in the literature using suitable starting materials. The starting materials of formulae II, m and IV are commercially available or can be prepared via a variety of known svnth-etic routes known in the literature.

[0107] For example, the starting materials used are arylalkylamines of formula (II)

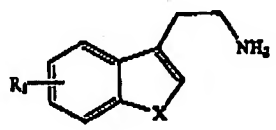


(II)

wherein R1 is as defined above and X is NH, O, CH2 or S.

[0108] When X is O, the amines of formula (II) can be the U.S. Pat. Specification No. 4,710,504. When X is $CH_2$, the compounds of formula (II) can be prepared as described in *J. Med. Chem.* 10 (1967) 856-859. When X is S, the compounds of formula (II) can be prepared by decarboxylation of the corresponding 3-(thianaphten-3-yl)-L-alanine.

[0109] Other starting materials used are compounds of formula (III)

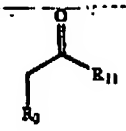


(II)

wherein $R_1$ is as defined above and X is NH, O, CH2 or S.

[0110] When X is O, the amines of formula (II) can be prepared, for example, according to the process disclosed in the U.S. Pat. Specification No. 4,710,504. When X is $CH_2$, the compounds of formula (II) can be prepared as described in *J. Med. Chem.* 10 (1967) 856-859. When X is S, the compounds of formula (II) can be prepared by decarboxylation of the corresponding 3-(thianaphten-3-yl)-L-alanine.

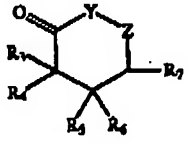
[0111] Other starting materials used are compounds of formula (III)



(III)

wherein $R_3$ is as defined above and $R_{11}$ is OH or halogen.

[0112] Furthermore, the starting materials used are compounds of formula (IV)



(IV)

wherein $R_3$-$R_7$ and Z are as defined above and Y is O or NH. Compounds of formula (IV) can be prepared according to the methods described in *Tetrahedron* 33 (1977) 1803-1808. Analogously, the corresponding acid chlorides can be used instead of lactones (Y=O). When $R_3$ and $R_5$ form a ring, compounds of formula (IV) are obtained by the partial reduction of their corresponding anhydrides.

[0113] In general, the compounds of formula (I), wherein X is NH, O or S, can be prepared e.g. analogously or according to the following reaction scheme 1:

9. A method according to claim 1, wherein X is O

10. A method according to claim 1, wherein X is S.

11. A method according to claim 1, which comprises the manufacture of a medicament for the treatment of a disorder of the central nervous system, diabetes, orthostatic hypotension, lipolytic disorder disorders, Raynaud's disease or male or female sexual dysfunctions.

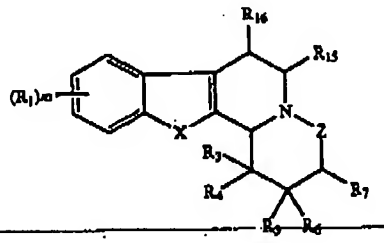
12. A method according to claim 11, wherein the disorder of the central nervous system is depression, anxiety disorder, post-traumatic stress disorder, schizophrenia, Parkinson's disease, or another movement disorder.

13. A method according to claim 1, wherein the compound is a selective alpha-2C antagonist.

14. A method according to claim 13 which comprises the treatment of a mental disorder propagated by stress, Parkinson's disease, depression, negative symptoms of schizophrenia, attention deficit hyperactivity disorder, post-traumatic stress-disorder, or anxiety disorder.

15. A compound of formula IA

IA



wherein,

X is $CR_2R_2'$, O or S;

Z is —$CHR_8$—$(CH_2)$n- or a single bond;

$R_1$ is hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halogen, halo$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO—, CN, $NO_2$, $NH_2$, mono- or di$(C_1$-$C_6)$alkylamino or carboxyl;

$R_2$ and $R_2'$ are independently H, hydroxy or $(C_1$-$C_6)$alkyl or $R_2$ and $R_2'$ form, together with the carbon ring atoms to which they are attached, a carbonyl group;

$R_3$ is H, hydroxy, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_6)$alkyl, aryl, aryl$(C_1$-$C_6)$alkyl, aryloxy, aryl$(C_1$-$C_6)$alkoxy, aryloxy$(C_1$-$C_6)$alkyl, aryl$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $NH_2$, amino$(C_1$-$C_6)$alkyl, mono- or di$(C_1$-$C_6)$alkylamino, mono- or di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-CO—, $(C_1$-$C_6)$alkyl-CO—O—, $(C_1$-$C_6)$alkyl-CO—O—$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO—, $(C_1$-$C_6)$alkoxy-CO—$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, carbamoyl, mono- or di$(C_1$-$C_6)$alkylcarbamoyl, carboxyl or $(C_1$-$C_6)$alkyl-S-$(C_1$-$C_6)$alkyl, wherein the said $(C_3$-$C_7)$cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being halo$(C_1$-$C_6)$alkyl, halogen, $(C_1$-$C_6)$alkoxy, $NH_2$, CN or $NO_2$, or one of $R_3$ or $R_4$ and $R_6$ together form a bond between the ring atoms to which they are attached;

$R_4$ is H, hydroxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy or $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl;

$R_5$ is H, hydroxy, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_7)$cycloalkyl, $(C_3$-$C_7)$cycloalkyl$(C_1$-$C_6)$alkyl, aryl, aryl$(C_1$-$C_6)$alkyl, aryloxy, aryl$(C_1$-$C6)$alkoxy, aryloxy$(C_1$-$C_6)$alkyl, aryl$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-CO—O—$(C_1$-$C_6)$alkyl-CO—O—$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, carbamoyl, mono- or di$(C_1$-$C_6)$alkylcarbamoyl, carboxyl or $(C_1$-$C_6)$alkyl-S—$(C_1$-$C_6)$alkyl, wherein the said $(C_3$-$C_7)$cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, $(C_1$-$C_6)$alkyl, halogen, $(C_1$-$C_6)$alkoxy, $NH_2$, CN or $NO_2$, or $R_4$ and $R_5$ form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring substituted with 1 to 3 substituent(s) Rg each independently being hydroxy, $(C_1$-$C_6)$alkyl, halogen, $NH_2$, $NO_2$, $(C_3$-$C_7)$cycloalkyl, hydroxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, mono- or di$(C_1$- $C_6)$alkylamino, mono- or di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, carboxyl, $(C_1$—$C_6)$alkyl-CO—, $(C_1$-$C_6)$alkyl-CO—O—, $(C_1$-$C_6)$alkoxy-CO—, $(C_1$-$C_6)$alkoxy-CO—$(C_1$-$C_6)$alkyl, carbamoyl mono- or di$(C_1$-$C_6)$alkylcarbamoyl or oxo;

$R_6$ is H, hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy or $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl or $R_6$ forms a bond between the ring atom to which it is attached and the ring atom to which $R_7$ is attached;

$R_7$ is H, hydroxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy or $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl;

$R_8$ is H,hydroxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy or $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl or, only when n is 0, $R_7$ and $R_8$ form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) Rio each independently being hydroxy, $(C_1$-$C_6)$alkyl, halogen, $NH_2$, $NO_2$, $(C_3$-$C_7)$cycloalkyl, hydroxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, mono- or di$(C_1$-$C_6)$alkylamino, mono- or di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, carboxyl, $(C_1$-$C_6)$alkyl-CO-, $(C_1$-$C_6)$alkyl-CO-O-, $(C_1$-$C_6)$alkoxy-CO—, $(C_1$-$C_6)$alkoxy-CO—$(C_1$-$C_6)$alkyl, carbamoyl, mono- or di$(C_1$-$C_6)$alkylcarbamoyl or oxo;.

$R_{10}$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, mono- or di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-CO—, $(C_1$-$C_6)$alkyl-CO—O—$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO—, $(C_1$-$C_6)$alkoxy-CO-$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-CO-$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, carbamoyl, mono- or di$(C_1$-$C_6)$alkylcarbamoyl or carboxyl;

$R_{11}$ is H or $(C_1$-$C_6)$alkyl;

substituents each independently being hydroxy, ($C_1$-$C_6$)alkyl, halogen, ($C_1$-$C_6$)alkoxy, $NH_2$, CN or $NO_2$, or $R_5$ and $R_6$ together form a bond between the ring atoms to which they are attached;

$R_6$ is H, hydroxy, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy or ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl or $R_6$ forms a bond between the ring atom to which it is attached and the ring atom to which $R_7$ is attached;

$R_7$ is H, hydroxy, ($C_1$-$C_6$)alkyl, hydroxY($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy or ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl;

$R_8$ is H,hydroxy, ($C_1$-$C_6$)alkyl, hydroxy($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy or ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl or, only when n is 0, $R_7$ and RN form, together with the carbon ring atoms to which they are attached, a condensed five to seven membered saturated carbocyclic ring unsubstituted or substituted with 1 to 3 substituent(s) $R_{10}$ each independently being hydroxy, ($C_1$-$C_6$)alkyl, halogen, $NH_2$, $NO_2$, ($C_3$-$C_7$)cycloalkyl, hydroxy($C_1$-$C_6$)alkyl, halo($C_1$-$C_6$)alkyl, amino($C_1$-$C_6$)alkyl, mono- or di($C_1$-$C_6$)alkylamino, mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, carboxyl, ($C_1$-$C_6$)alkyl-CO—, ($C_1$-$C_6$)alkyl-CO—O—, ($C_1$-$C_6$)alkoxy-CO—, ($C_1$-$C_6$)alkoxy-CO—($C_1$-$C_6$)alkyl, carbamoyl, mono- or di($C_1$-$C_6$)alkylcarbamoyl or oxo; $R_9$ is hydroxy, ($C_1$-$C_6$)alkyl, halogen, $NH_2$, $NO_2$, ($C_3$-$C_7$)cycloalkyl, hydroxy($C_1$-$C_6$)alkyl, halo($C_1$-$C_6$)alkyl, amino($C_1$-$C_6$)alkyl, mono- or di($C_1$-$C_6$)alkylamino, mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, carboxyl, ($C_1$-$C_6$)alkyl-CO—, ($C_1$-$C_6$)alkyl-CO—O—, ($C_1$-$C_6$)alkoxy-CO—, ($C_1$-$C_6$)alkoxy-CO-($C_1$-$C_6$)alkyl, carbamoyl mono- or di($C_1$-$C_6$)alkylcarbamoyl or oxo;

$R_{10}$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, hydroxy($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, hydroxy($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, halo($C_1$-$C_6$)alkyl, amino($C_1$-$C_6$)alkyl, mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-CO—, ($C_1$-$C_6$)alkyl-CO—O—($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy-CO—, ($C_1$-$C_6$)alkoxy-CO-($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, carbamoyl, mono- or di($C_1$-$C_6$)alkylcarbamoyl or carboxyl;

$R_{10}$ is H or ($C_1$-$C_6$)alkyl;

$R_7$ and $R_8$ are attached to the carbon ring atoms, which are adjacent;

m is 0 to 2; and

r is 1 to 3;

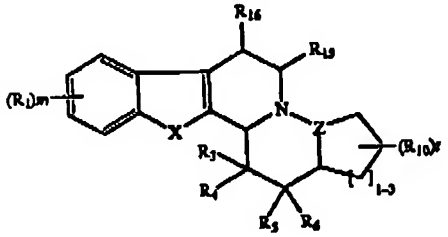
or a pharmaceutically acceptable salt or a ester thereof, with the provisos, that the compound is not 10-methyl-5,7,7a,8,9,10,11,11a,11 b,12-decahydro-6H-6a,12-diaza-indeno[1,2-a]fluorene; 3-hydroxy-1,2,3,4,4a,5,6,7,8,13,13b,13c-dodecahydro-6a,13-diaza-indeno[1,2-c]phenanthrene-4-carboxylic acid methyl ester; methyl-3-ethyl-1,2,3a,4,6,7,12b,12c-octahydro-3H,12H-indolo[2,3-g]cyclopent[a]indolizine-2-carboxylate; methyl-1,2,3a,4,6,7,12b,12c-octahydro-3H,12H-indolo[2,3-g]cyclopent[a]indolizine-2-carboxylate or 12c-ethyl-1,3a,4,6,7,12b,12c-octahydro-cyclopent[1,2]indolizino[8,7-b]indol-3(2H)-one.

27. A compound according to claim 26, wherein r is 1 and $R_9$ is H, hydroxy, ($C_1$-$C_6$)alkyl or hydroxy($C_1$-$C_6$)alkyl.

28. A compound according to claim 26, wherein the compound is 3,4,4aβ,5,6,7,8,13,13bβ,13cα-decahydro-2H-6a,13-diaza-indeno[1,2-c]phenanthren-1-one, 1,2,3,4,5,6,7,8,13,13b-decahydro-6a,13-diaza-indeno[1,2-c]phenanthrene, acetic acid 1α,2,3,4,4aαβ,5,6,7,8,13,13bβ,13cα-dodecahydro-6a,13-diaza-indeno[1,2-c]phenanthren-1-yl ester or acetic acid 1β,2,3,4,4aβ3,5,6,7,8,13,13bβ,13cα-dodecahydro-6a,13-diaza-indeno[1,2-c]phenanthren-1-yl ester.

29. A compound of formula ID

ID



wherein,

X is $NR_2$;

$R_2$ is H;

Z is —CH—($CH_2$)n-;

n is 0;

$R_1$ is hydroxy, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, halogen, halo($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy-CO—, CN, $NO_2$, $NH_2$, mono- or di($C_1$-$C_6$)alkylamino or carboxyl;

$R_3$ is H, hydroxy, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, hydroxy($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, hydroxy($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, ($C_3$-$C_7$)cycloalkyl, ($C_3$-$C_7$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl, aryloxy, aryl($C_1$-$C_6$)alkoxy, aryloxy($C_1$-$C_6$)alkyl, aryl($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, halo($C_1$-$C_6$)alkyl, $NH_2$, amino($C_1$-$C_6$)alkyl, mono- or di($C_1$-$C_6$)alkylamino, mono- or di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-CO—, ($C_1$-$C_6$)alkyl-CO—O—, ($C_1$-$C_6$)alkyl-CO—O—($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy-CO—, ($C_1$-$C_6$)alkoxy-CO—($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy-CO—($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, carbamoyl, mono- or di($C_1$-$C_6$)alkylcarbamoyl, carboxyl or ($C_1$-$C_6$)alkyl-S-($C_1$-$C_6$)alkyl, wherein the said ($C_3$-$C_7$)cycloalkyl or aryl is unsubstituted or substituted with 1 or 2 substituents each independently being hydroxy, ($C_1$-$C_6$)alkyl, halogen, ($C_1$-$C_6$)alkoxy, $NH_2$, CN or $NO_2$, or one of $R_3$ or $R_4$ and $R_6$ together form a bond between the ring atoms to which they are attached;

$R_4$ is H, hydroxy, ($C_1$-$C_6$)alkyl, hydroxy($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy or ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl;

$R_5$ is H, hydroxy, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkoxy($C_1$-$C_6$)alkyl, ($C_3$-$C_7$)cycloalkyl, ($C_3$-$C_7$)cycloalkyl($C_1$-$C_6$)alkyl, aryl,